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QUALITATIVE ANALYSIS OF DELAYED-CONCENTRATION IN OREGONATOR-BASED CHEMICAL OSCILLATORS

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ABSTRACT

Beulosuv-Zhabotonksiy reaction is pure chemical reaction that exhibits sustained and relaxed oscillations, which are analogous to observed oscillations in many biological systems. The reaction is very complicated, however, its oscillatory mechanism is represented by a simple model, called the Oregonator. Since delays naturally appear in chemical reactions and they are often responsible for presence of complex behaviours, delay effects in Beulosuv-Zhabotonksiy reaction should be considered to better explain the mechanism of some biochemical oscillations. In this work, qualitative and asymptotic analysis of the Oregonator model by taking into account the delays arising due to the physical constraints will be considered. Some numerical results will given to present some certain properties of the considered model.

Keywords: Biochemical oscillations, Time-delay systems, BZ reaction

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1. INTRODUCTION

Delays naturally appear in many engineering applications, biological, and chemical processes, due to the transportation and propagation phenomena, for instance, transportation of information or energy in interconnected systems requires some amount of time, signals in real-time control applications can not be computed instantaneously, mass transfer in processes occurs after a finite interval (see, [1] and references there in for a wide survey). Besides the above phenomena, since delay-differential equations (DDEs) have richer mathematical framework compared to ordinary differential equations (ODE), modelling systems in the field biology and chemistry by using DDEs may introduce certain benefits from the numerical point of view [2]. In addition, as pointed in [3], DDEs may lead to describe chemical reactions by a fewer concentration variables than the classical mass-action law.

Chemical reactions are often modelled by law of mass-action, which states that the rate of a reaction is proportional to the product of concentrations of the reactants by assuming all the stoichiometric coefficients of the reactants are one [4]. Then, the resulting dynamic model is described by polynomial ODEs, where their solutions are non-negative for non-negative initial conditions [5]. Note that, since dynamic variables of a kinetic equation obtained by mass-action laws correspond to the concentrations of the species in the reaction, non-negative initial conditions must yield non-negative solution from the physical point of view. However, mass-action laws may not be sufficient in presence of delays, which naturally appear in dynamics of chemical reactions due to the propagation phenomena. In fact, delays in chemical reactions are often sufficiently small, hence, they may be neglected. However, delay presence in system's dynamics is often responsible for unexpected behaviours [1]. In addition, as mentioned in [6], delays induced behaviours in complex chemical reactions should be considered to better understand the dynamics of such reactions.

Belousov-Zhabotinsky reaction, called BZ reaction, is a very complex chemical reaction involving dozens of elementary steps and exhibiting various type of behaviours such as steady-state, periodic, and chaotic. The reaction, in short, consists of two different processes, say Process A and B, in one system such that

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only one of them dominates the reaction depending on the Bromide ion concentration in the reaction at any time. Process A dominates the reaction when the Bromide ion concentration is sufficiently high, and the Bromide ion is consumed monotonically during this process. Then, whenever the concentration reduces below some certain level, Process B starts to dominate the reaction. The oscillatory mechanism origins that Bromide ion is indirectly produced in Process B, hence, control of the reaction is returned to Process A. In [7], this mechanism is represented by a simple model, called the Oregonator model. Since oscillatory behaviour of the BZ reaction is analogous to many real biological oscillators, the reaction mechanism is accepted as a prototype for biochemical oscillators [8, 9, 10]. Since biochemical oscillations, which are common in all biological organizations, play key roles in a variety of important processes, including circadian regulation, metabolism, neuronal firing, and cardiac rhythms [10, 11, 12], it is important to comprehend its mechanism. Note, even these behaviors have been known for a long time, the underlying mechanism is still not clear [11, 13]. Since BZ reaction has rich complex dynamics, mechanism of some biochemical oscillations may be better explained if delays are taken into account.

To the best knowledge of the author, there exists only limited works on delay effects in the Oregonator model. Most of them are considered to describe the mechanism with a fewer chemical concentration variables. In [6], two different models are proposed to describe the oscillatory mechanism by using DDEs, however, only one of them, which does not satisfy the delay mass-action law, exhibits oscillatory behavior at the non-trivial equilibrium point. By inspiring the work of [6], another delayed-Oregonator model is proposed in [3] such that the model satisfies the delay mass-action laws and exhibits qualitatively the same oscillatory behavior with the Oregonator model. Different than these works, in [14], a two-delay Oregonator model is proposed to take into account the delay effects arising due to the physical constraints while ensuring the oscillatory behavior in the mechanism. One of these delays, called ``delayed-activation'', has the same role as in [3], and the other one, called ``delayed-concentration'', is introduced due to the physical constraints. Note, ``delayed-concentration'' term is also used in [6], however, its role in [14] is completely different in the sense of modelling and physical point of view. As shown by numerical results, oscillatory behavior of the two-delay Oregonator qualitatively match with the model in [7] if the activation and concentration delays are relatively ``small''.

In this work, in order to better understand the arising complex dynamics of BZ in presence of delays introduced by the specific physical constraints will be considered. It should be noted that despite the advantages of use of DDEs in the field of bioscience, mathematical solution of a DDE is more difficult compared to ODE. Solution of a DDE requires an infinite set of initial history function, therefore, it is not trivial to ensure positivity of the solution, which is required for DDEs describing the chemical reactions. In addition, characteristic polynomial of a system described by DDEs may have infinitely many zeros. In Section 2, chemical kinetics of the considered Oregonator model will be given. In addition, by use of delay mass-action law, its dynamic and asymptotic properties will be presented. Then, some numerical results will be presented in Section 3 and the paper will be completed by some concluding remarks in Section 4.

2. MODEL OF THE MECHANISM

From [7], the reaction steps of the irreversible Oregonator model is as given below

$$A + Y \overset{k_1}{\rightarrow} X + O \qquad (R_1)$$
$$X + Y \overset{k_2}{\rightarrow} 2O \qquad (R_2)$$
$$B + X \overset{k_3}{\rightarrow} 2X + Z \qquad (R_3)$$
$$2X \overset{k_4}{\rightarrow} A + O \qquad (R_4)$$
$$Z \overset{k_5}{\rightarrow} fY, \qquad (R_5)$$

where A, B are assumed to be constant chemical species, Y (Bromide ion), X (Bromous acid), and Z (Cerium (IV)) are chemical variables, O is some chemical product, k_i, $i = 1, ..., 5$, is the positive rate constant, and, f is a stoichiometric factor. By using the mass-action law, as given in [6], dynamic model of the Oregonator model is obtained as given below:

$$\dot{X}(t) = k_1AY(t) - k_2X(t)Y(t) + k_3AX(t) - 2k_4X(t)^2 \quad (1a)$$
$$\dot{Y}(t) = -k_1AY(t) - k_2X(t)Y(t) + k_5fZ(t) \quad (1b)$$
$$\dot{Z}(t) = k_3BX(t) - k_5Z(t), \quad (1c)$$

where $k_1 = 1.34M^{-1}sec^{-1}$, $k_2 = 1.6 \times 10^9M^{-1}sec^{-1}$, $k_3 = 8 \times 10^3\ M^{-1}sec^{-1}$, $k_4 = 4 \times 10^7M^{-1}sec^{-1}$, $k_5 = 1\ sec^{-1}$, $f = 1$, and $A = B = 0.06$ [7].

It is mentioned in [15], the reactants in a chemical reaction are not necessarily to react whenever the activation energy is provided. In addition to such a time lag, it is not physically possible to maintain the required activation energy instantaneously. In order to take into account these type of delays in the BZ reaction, the Oregonator model can be expressed, by replacing (R_1) with

$$A + Y \overset{k_1}{\rightarrow} X(t+\tau) + O(t+\tau), \qquad (dR_1)$$

which implies that X and O appear after τ units. The recent mechanism, which corresponds to replacing reaction step R_1 by dR_1, is more realistic compared to the Oregonator model from the physical point of view.

Remark 1 Note that, the reaction mechanism consists of five elementary steps, and, delay may introduced all these steps due to transportation phenomena. Note, as seen from $R_1 - R_5$, since O is not on the reactant part and A is assumed to be constant, the considered chemical variables appear only in R_1, R_3, and R_5. In addition, since the role of R_5 in the mechanism can be considered to provide a negative delayed feedback [6], and, the reaction rate constant in R_3, which corresponds to k_3, is ``sufficiently large'' than k_1, R_1 becomes the slowest step. Furthermore, since the reaction starts whenever the present Bromide ion starts to decrease, taking into account the existing time lag in R_1 is more meaningful compared to elementary steps.

By delayed mass-action laws, the kinetic scheme of delayed Oregonator model, which consists of the steps $(dR_1), R_2 - R_5$, can be described by the following DDEs

$$\dot{X}(t) = k_1AY(t-\tau) - k_2X(t)Y(t) + k_3AX(t) - 2k_4X(t)^2 \quad (2a)$$
$$\dot{Y}(t) = -k_1AY(t) - k_2X(t)Y(t) + k_5fZ(t) \quad (2b)$$
$$\dot{Z}(t) = k_3BX(t) - k_5Z(t). \quad (2c)$$

Since it will be more convenient to use dimensionless variables, the dimensionless DDEs can be obtained as follows:

$$\dot{x}(\theta) = \delta(y(\theta - h) - x(\theta)y(\theta) + x(\theta) - \rho x(\theta)^2) \quad (3a)$$
$$\dot{y}(\theta) = 1/\delta(-y(\theta) - x(\theta)y(\theta) + fz(\theta)) \quad (3b)$$
$$\dot{z}(\theta) = \gamma(x(\theta) - z(\theta)), \quad (3c)$$

where, $\theta = \sqrt{k_1k_3}At$, $\delta = \frac{k_3}{k_1}$, $\gamma = \frac{k_5}{A\sqrt{k_1k_3}}$, $\rho = \frac{2k_1k_4}{k_2k_3}$, $h = \sqrt{k_1k_3}A\tau$, $x = \frac{k_1}{k_2}AX$, $y = \frac{k_3}{k_2}AY$, $z = \frac{k_1k_3}{k_2k_5}Z$. In the sequel, first, presence of a positive equilibrium point for the dynamic model described in (3a-3c) will be presented. Note, since the dynamic variables in (2a-2c) correspond to instantaneous concentration of the considered chemical variables, the equilibrium point of the model should be positive. Then, the positivity of the solutions for positive initial history function will be shown, and asymptotic properties of the model will be given.

Proposition 1. The model described by dimensionless DDEs in (3a)-(3c) has only one positive equilibrium point (x^*, y^*, z^*), where

$$y^* = f\frac{x^*}{1+x^*} \tag{4}$$

and

$$z^* = x^* = \frac{(\rho+f-1)-\sqrt{(\rho+f-1)^2+4(1+f)q}}{-2q} \tag{5}$$

Proof Let (x^*, y^*, z^*) be a solution of $(\dot{x}(\theta), \dot{y}(\theta), \dot{z}(\theta)) = 0$. Then,

$$y^* - x^*y^* + x^* - \rho(x^*)^2 = 0 \tag{6}$$
$$-y^* - x^*y^* + fz^* = 0 \tag{7}$$
$$-x^* + z^* = 0. \tag{8}$$

From (7-8), since $z^* = x^*$ and $y^* = f\frac{x^*}{1+x^*}$, by (6),

$$-\rho(x^*)^2 - (\rho+f-1)x^* + (1+f) = 0. \tag{9}$$

Note, since it is obvious that

$$\sqrt{(\rho+f-1)^2 + 4\rho(1+f)} > (\rho+f-1),$$

the positive solution of (9) is obtained as in (5).

Proposition 2. Solution of the DDEs in (3a-3c) is positive for a positive initial history function.

Proof By contradiction, assume that the DDEs has a non-positive solution for some positive initial history function, which implies that $x(\hat{t}) > 0, y(\hat{t}) > 0$, and $z(\hat{t}) > 0, \hat{t} \in [-h, 0]$. Now, from (3c), since

$$z(\theta) = e^{-\gamma\theta}z(0) + \int_0^\theta e^{-\gamma(\theta-\tau)}x(\tau)d\tau, \qquad \theta > 0, \tag{10a}$$

then, $z(\theta) \le 0$ only if there exists a positive θ_1, $\theta_1 \le \theta$, such that $x(\theta_1) \le 0$, since $z(0) > 0$. Then, the positivity of initial history function yields that there exists a positive θ_2, where $\theta_2 \le \theta_1$, such that $x(\theta_2) = 0$. From (3a), since

$$\dot{x}(\theta_2) = \delta y(\theta_2 - h), \tag{10b}$$

$x(\theta_1) \le 0$ only if $y(\theta_2 - h) < 0$. However, the latter inequality holds only if there exists a positive θ_3, such that $\theta_3 \le \theta_2 - h$ and $y(\theta_3) = 0$. However, from (3b), since,

$$\dot{y}(\theta_3) = \frac{fz(\theta_3)}{\delta} > 0, \tag{10c}$$

then, $z(\theta)$ can not be non-positive. Furthermore, by using (10b-10c), it can be easily shown that $x(\theta)$ and $y(\theta)$ can not be non-positive.

Proposition 3. The characteristic function of the linearized model given in (3a-3c) has two positive real zeros in the right-half plane for $h \ge 0$.

Proof By linearizing (3a-3c) around the positive equilibrium point (x^*, y^*, z^*) given in (4-5), the characteristic function of the model can be written as:

$$\Delta(\lambda; h) = \lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 + e^{-h\lambda}(q_1\lambda + q_0) \tag{11}$$

where λ is a complex number, and

$$a_2 = \gamma + \frac{1}{\delta}(1 + x^*) + \delta(y^* + 2\rho x^* - 1) \tag{12a}$$
$$a_1 = (1 + x^*)(2\rho x^* - 1) + y^* + \gamma\left(\frac{1}{\delta}(1 + x^*) + \delta(y^* + 2\rho x^* - 1)\right) \tag{12b}$$
$$a_0 = \big((1 + x^*)(2\rho x^* - 1) + y^* + fx^*\big)\gamma \tag{12c}$$
$$q_1 = y^* \tag{12d}$$
$$q_0 = (y^* - f)\gamma. \tag{12e}$$

By the given parameters above, from (12a-12e), it can be shown that $a_2 > 0,\ a_1 < 0,\ a_0 > 0,\ 1 > q_1 > 0,\ q_0 < 0,\ a_0 + q_0 > 0$, and, $a_1 + e^{-h\sigma}q_1 < 0$, for $\sigma > 0$. Then, since $e^{-h\sigma} < 1, h \geq 0$, by Descartes's sign rule, $\Delta(\sigma; h)$ =0 only for two real positive σ.

Proposition 4. The characteristic function of the model has no zeros in the right-half plane for $h \geq 0$ if $f \leq 1/2$.

Proof Let us define

$$d(\lambda) \coloneqq \lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 \tag{13}$$

where $a_2,\ a_1$ and a_0 are defined as in (12a-12c). Then, since $a_2 > 0$ for positive f, in addition, as seen in Figure 1(a), $a_2 a_1 - a_0$ is positive for $f \leq \frac{1}{2}$, then, by Hurwitz criterion, it can be shown that $d(\lambda) \neq 0, \lambda \in \mathbb{C}_+$. Then, since the characteristic function given in (11) can be written as

$$\Delta(\lambda; h) = d(\lambda)\left(1 + e^{-h\lambda}\frac{q_1\lambda + q_0}{d(\lambda)}\right) \tag{14}$$

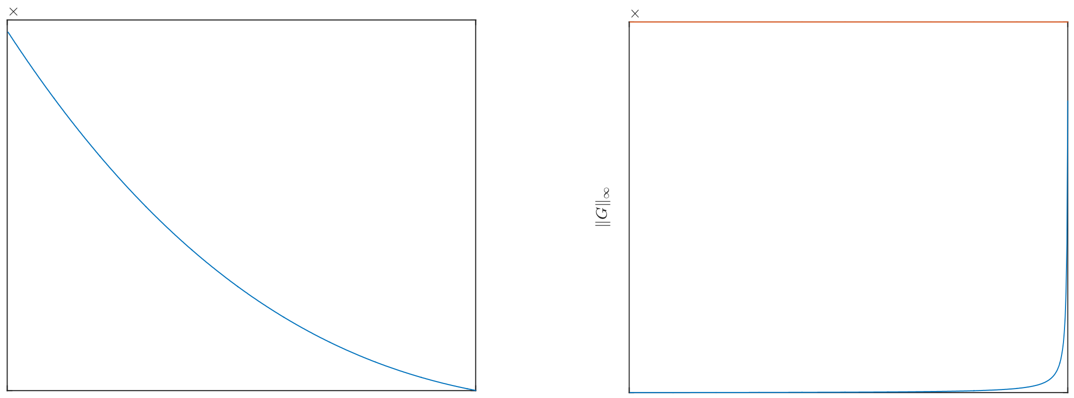
then, the characteristic function has zeros in the right-half-plane ($\mathbb{C}_+$) only if

$$e^{-h\lambda}\frac{q_1\lambda + q_0}{d(\lambda)} = -1 \tag{15}$$

holds for some $\lambda \in \mathbb{C}_+$. Note that, since $d(\lambda) \neq 0, \lambda \in \mathbb{C}_+$,

$$G(\lambda; h) \coloneqq e^{-h\lambda}\frac{q_1\lambda + q_0}{d(\lambda)}, \tag{16}$$

is analytic and bounded in the open-right-half-plane for $h \geq 0$. In addition as shown in Figure 1(b), $\|G(\lambda; h)\|_\infty = \sup_{\omega \in \mathbb{R}}|G(j\omega; h)| < 1,\ h \geq 0$. Then, by the maximum modules theorem [16], the characteristic function has no zeros in the right-half-plane.



(a) (b)

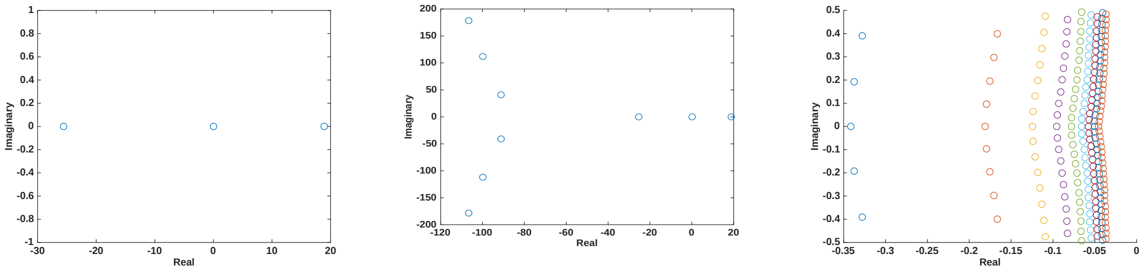
Figure 1. Stability condition of the characteristic function while f versus in $\left[0,\frac{1}{2}\right]$: (a), $(a_2a_1 - a_0)$ while f versus in $\left[0,\frac{1}{2}\right]$ (b) $||G(\lambda; h)||_\infty$ while f versus in $\left[0,\frac{1}{2}\right]$, $h \geq 0$.

3. NUMERICAL RESULTS

In this section, some numerical results will be presented to explain the asymptotic properties of the model described by dimensionless DDEs in (3a-3c). In addition, numerical solutions of the model will be presented to discuss dynamic behaviour of the model.

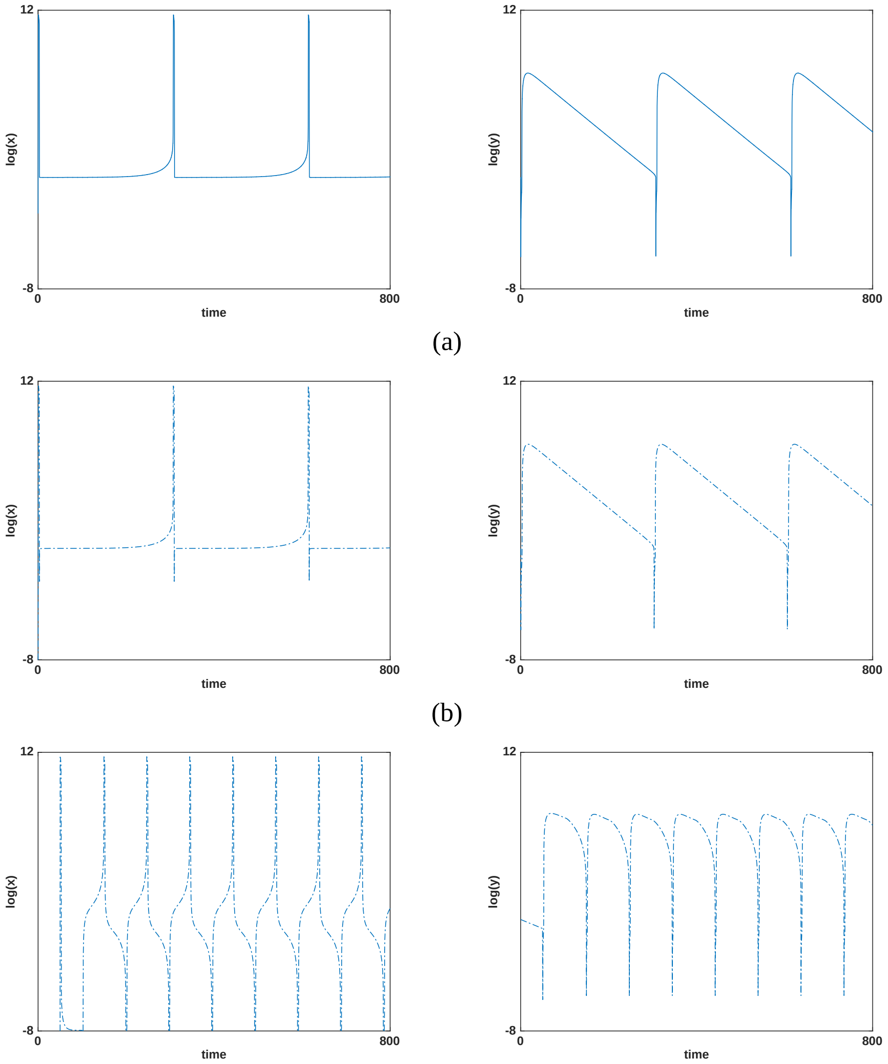
The characteristic function of the model, which is given in (11) has infinitely many zeros in the complex-plane, however, only finitely many of them appear in the right-half plane [17]. Since their computation is difficult, by using QPmR [18], zeros of the characteristic function will be presented only a certain interval. As shown in Figure 2(a), the Oregonator model in [6] has two real zeros in the right-half-plane. As discussed in Proposition 3 and shown in Figure 2(b), presence of delay does not change the right-half-plane zeros of the Oregonator model in [6], however, it introduces additional zeros, which are infinitely many. As shown in Figure 2(c), the characteristic function has no zeros in the right-half-plane while h versus in [0,20] and $f = \frac{1}{2}$ (see, Proposition 4). In addition, as seen in the figure, as $h \rightarrow \infty$, left-half-plane zeros of the characteristic function approaches to the imaginary axis.

In Figure 3, numerical solutions of the Oregonator model in [6] and numerical solutions of (3a-3c) are presented for a chosen positive initial condition. As seen in these figures, numerical solutions are positive, as shown in Proposition 2, and they exhibit oscillatory behaviour for the considered set of parameters and delay values. In addition, the oscillatory behaviour of the Oregonator model in [6] and delayed-Oregonator model qualitatively match for ``small'' delay values. If delay is taken "sufficiently" large, the oscillatory behavior still exists. As seen by comparing Figure 3(b) and Figure 3(c), the frequency of the oscillations increases if delay increases.



(a) (b) (c)

Figure 2. Zeros of the Characteristic function for (a) h=0 f=1, (b) h=0.1, f=1, (c) f=1/2 h versus in [0,20]



(a)

(b)

(c)

Figure 3. Numerical solutions of ODEs and DDEs. . In (a), $f = 1$, h= 0 (b) f = 1 , h= 0.05 (c) f = 1, h= 5 and the other parameters are kept same and the initial condition is taken as $(0,1,0)$.

4. CONCLUSION

In this work, qualitative analysis of a delayed-Oregonator-based chemical oscillator is presented to discuss the delay effects in chemical reactions. The dynamic model of the considered mechanism is obtained by using delay-mass action laws. It is shown that the model is meaningful from the physical point of view, since, it has unique positive equilibrium point, in addition, solution of the corresponding DDEs is positive for positive initial history function. It is shown that delayed-concentration does not effect the asymptotic stability properties of the reaction mechanism, but it increases the frequency of oscillatory behaviour.

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